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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,994	08/03/2001	Michael R. Bowman	GIN-5381	7090

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EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,994	BOWMAN, MICHAEL R.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- Th MAILING DATE of this communication app ars on th cover sheet with the correspondenc addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5-7,12,16,17,30 and 31* is/are pending in the application.

4a) Of the above claim(s) *7,12,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 5-6, 30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 12, 2003 has been entered.

Status

2. Claims 2, 5-7, 12, 16, 17, 30-31 are pending.

Claims 2, 5-6, 30 and 31 are rejected.

Claims 7, 12, 16 and 17 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 2, 5-6, 30 and 31 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of nucleic acids termed EBI-3-alt in the specification and are further defined by reference to SEQ ID Nos: 1-3. An important point is that while the name of the protein is EBI, reminiscent of Epstein Barr induced,

there is no evidence found in the specification that the current nucleic acid or protein are induced by infection of cells with Epstein Barr virus. Thus, no utility can be based upon this inference since there is no apparent evidence that this protein is, in fact, induced by Epstein Barr virus.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The only cited utilities identified by the examiner are to detect the EBI-3-alt nucleic acid or protein itself, to make antibodies and to screen drugs. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this specific EBI-3-alt protein are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence in the specification itself teaches that the EBI-3-alt is homologous both to a cytokine receptor and to a nitrous oxide reductase (see page 65, lines 27-36 of specification). This extreme disparity in possible activities for the protein highlights the absence of any substantial utility.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves

lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). There is no data in the specification linking this gene to any disease or to any specific biological function. The only element known is that the protein may be induced by the Epstein Barr virus, but this provides no substantial utility and no evidence that this induction occurs was found in the specification. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, there is no suggestion for any particular use of the EBI-3-alt nucleic acids as distinguished from any other nucleic acid which encodes an open reading frame. The current specification simply recites a laundry list of every possible generic use to which a nucleic acid and the protein encoded by that nucleic acid could be put. However, there is not a single substantial use related to the EBI-3-alt protein or nucleic acid itself.

Specific Utility

Further, none of the laundry list of utilities identified in the specification are specific to the EIB-3-alt protein or nucleic acid. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, there is not even such a general prediction. There is no disclosure of any condition which can be diagnosed and hence, no specific utility. In particular, there is no evidence that the protein or nucleic acid are induced by Epstein Barr virus. There is no disclosure of any utility whatsoever which can be

performed by the EBI-3-alt protein or nucleic acid which is specific to those molecules and which could not be performed using any nucleic acid or protein that exists.

Finally, with regard to the utility analysis, the current situation directly tracks Example 4 of the utility guidelines, where a protein of entirely unknown function was characterized as lacking utility.

Response to Arguments – 101 Rejection

5. Applicant's arguments filed December 12, 2003 have been fully considered but they are not persuasive.

Applicant begins by relying upon the utility of EBI-3 for utility. However,the current protein is NOT EBI-3, but rather EBI-3 alt. Thus, evidence regarding the activity or function of EBI-3 does not provide any significant evidence for the patentable utility of EBI-3 alt. So the utility claimed by Applicant is the limited structural analogy to a different protein which may have utility. This is lesser level of utility than the amount rejected by the Supreme court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966). In Brenner, a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. So unlike in the current case, the related compound had a clear utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that

an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a polynucleotides encoding a protein which has no identified activity. The function of the EBI-3-alt gene and its resulting protein are as yet undetermined with no known function or biological significance. Until some actual and specific significance can be attributed to the EBI-3-alt protein identified in the specification, or the EBI-3-alt gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date directly consistent with *Brenner v. Manson*.

Applicant further argues that this case is similar to the utility guidelines at example 10. Applicant is incorrect. The current case is significantly different from example 10 because there is no listed function for the related protein, and there is no expectation of any particular utility for EBI-3-alt. Further, the reliance on the identity underlies the fundamental problem in this application. The identity is not, as Applicant states, to an Epstein Barr virus component, but rather to a human nucleic acid, EBI-3. As noted in the rejection, the homology is to two entirely different types of protein, one

of which is a cytokine receptor and the other of which is a nitrous oxide reductase. There is no evidence or teaching that the actually protein has either of those activities. Further, with regard to EBI-3 itself, the only disclosed utility for this protein is that it is induced by the Epstein Barr virus. Activation of proteins is well known to be exquisitely sensitive and specific, with different allelic variants being activated at different times in cell cycle, in development or in response to extracellular events. This differential expression is appreciated by the specification itself, at page 31, lines 1-14, where the specification recognizes "tissue specific" regulatory sequences. Therefore, there is no reason to believe that simply due to some level of homology, the current protein is activated by Epstein Barr virus or would serve as a marker for that virus.

Second, Applicant relies upon a 1978 text, (not submitted) and a 1997 paper (not submitted) as well as the utility guidelines to support the point that homology alone is predictive of utility. As noted in the enablement rejection below, a 2001 paper shows that homology is not predictive of function in many instances and provides evidence of such an instance. Also, this argument is not persuasive because it fails to address the central question. Homology, as in the case of ligases, may be predictive, where there are known domains in the protein with known properties which yield known enzymatic effects. This situation is not like the ligase example, but is much more similar to Example 12 of the Guidelines, where a "receptor" was found not to have utility because there was no real world context of use for the receptor. In the current case, unlike the guideline example, we do not even have the receptor itself. EBI-3 would be the receptor the guidelines would address. Here we simply have a protein that is

homologous to the receptor. This protein has no utility because there is no known "real world" use for the protein. Applicant has not provided any such "real world" use.

The question at issue is whether or not the broad general assertion that the claimed nucleic acids encode an EBI-3-alt protein which might be used for *some* application in the absence of a disclosure of *which* application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria and lacks utility. *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.'). This is precisely the attempt of this Applicant. This Applicant is attempting to induce the office into a guessing game in which the actual use of EBI-3-alt will be determined by someone else, and from whom this Applicant will then attempt to extract payment once a "real world" use is identified.

So contrary to Applicant's arguments, the patent statue, as interpreted by the Supreme Court in Brenner v. Manson, requires specific benefit in currently available form. No such specific benefit is present in this case.

For these reasons, the utility rejection is maintained.

Claim Rejections - 35 USC § 112 - Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 2, 5-6, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to nucleic acids which encode the EBI-3-alt protein. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass a variety of nucleic acids which may encode the EBI-3-alt protein, including alternatively spliced variants, nucleic acids which encode related proteins and a variety of mismatches based upon the 75% homology language. An important point is that while the name of the protein is EBI, reminiscent of Epstein Barr induced, there is no evidence found in the specification that the current nucleic acid or protein are induced by infection of cells with Epstein Barr virus. Thus, no utility can be based upon this inference since there is no apparent evidence that this protein is, in fact, induced by Epstein Barr virus.

Quantity of Experimentation

The quantity of experimentation in this area is very large since there is significant variability in the effect and function of proteins in living organisms. It is a truism that each protein has a different function in the cell and in the current situation, no use has been identified for the EBI-alt-e protein. Thus, in order to make any use of the protein, it's function in the cell must first be identified. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The prior art contains no precise match for the EBI-3-alt protein and therefore the protein and nucleic acid cannot be enabled based upon prior art disclosures. Birkenbach teaches a sequence which has significant homology with the EBI-3-alt

nucleic acid (it is noted that that patent issued prior to the current utility guidelines). The homology evidence presented in the specification indicates a relationship with two extremely divergent proteins, one a chemokine receptor and the other an enzyme involved in sulfur metabolism. Thus, the ordinary practitioner would have no expectation regarding the function of the EBI-3-alt protein and nucleic acid. It is extremely unpredictable what function a protein or nucleic acid will have, even when there is very good homology data. For example, Thrower et al (Trends Pharm. Sciences (2001) 22 (11) 580-6) notes regarding some inositol receptors that "Although these receptor isoforms possess high homology, interesting differences in their Ca2+ dependence, Ins(1,4,5)P3 sensitivity and subcellular distribution exist, implying distinct cellular roles. (abstract)". Thus, even where there is extremely high sequence homology, the proteins may have distinct physiological roles. In the current case, where the homology is lower and is related to two extremely divergent types of proteins, the physiological role is significantly unpredictable.

Working Examples

The specification has no working examples which disclose the function of the EBI-3-alt protein or nucleic acid.

Guidance in the Specification.

The specification has an abundance of generic guidance regarding uses for the EBI-3-alt protein and nucleic acid, but lacks any specific or substantial use. There is no disease or condition identified which is associated with this protein or nucleic acid, there is no physiological or cellular role identified for this protein or nucleic acid and there is

no function whatsoever which has been associated with the EBI-3-alt protein or nucleic acid.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to use the product of the claim as broadly written.

Response to Arguments – Enablement

8. Applicant's arguments filed December 12, 2003 have been fully considered but they are not persuasive.

Applicant arguments were not found persuasive for the reasons given above. Therefore, the enablement rejection is maintained.

Claim Rejections - 35 USC § 112 – Written Description

9. The rejection of claims under 35 U.S.C. 112, first paragraph, regarding written description is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

10. The rejection of claims 1, 3-6, 26 and 27 under 35 U.S.C. 102(b) is withdrawn in view of the amendment.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634